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NI et al.  
Appl. No. 09/042,583

### Amendments

The Examiner is respectfully requested to enter the following amendments.

#### ***Inventorship:***

Please delete Jeffery Su as an inventor.

#### ***In the Claims:***

Please cancel, without prejudice to or disclaimer of the subject matter thereof, claims 19, 21, 62-78, 80, 85, 101, 110, 154, 170-175, 190, and 210. Applicants reserve the right to pursue the canceled claims in related applications.

Please amend the claims as follows:

35. (Once Amended) An isolated polynucleotide comprising a first nucleic acid at least 90% identical to a second [reference] nucleic acid encoding amino acids 1 to 360 of SEQ ID NO:2.

C 36. (Once Amended) The isolated polynucleotide of claim 35, wherein said first nucleic acid is at least 95% identical to said second [reference] nucleic acid.

37. (Once Amended) The isolated polynucleotide of claim 36, which [comprises a nucleic acid encoding] encodes amino acids 1 to 360 of SEQ ID NO:2.

39. (Once Amended) The isolated polynucleotide of claim 35, wherein said second [reference] nucleic acid encodes amino acids -50 to 360 of SEQ ID NO:2.

40. (Once Amended) The isolated polynucleotide of claim 39, which [comprises a nucleic acid encoding] encodes amino acids -50 to 360 of SEQ ID NO:2.

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41. (Once Amended) The isolated polynucleotide of claim 40, which comprises nucleotides 133 to 1362 of SEQ ID NO:1.

42. (Once Amended) The isolated polynucleotide of claim 39, wherein said second [reference] nucleic acid encodes amino acids -51 to 360 of SEQ ID NO:2.

43. (Once Amended) The isolated polynucleotide of claim 42, which [comprises a nucleic acid encoding] encodes amino acids -51 to 360 of SEQ ID NO:2.

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45. (Once Amended) The isolated polynucleotide of claim 42, wherein said second [reference] nucleic acid is SEQ ID NO:1.

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47. (Once Amended) The isolated polynucleotide of claim 35, wherein said first nucleic acid encodes a polypeptide which binds [a Tumor Necrosis Factor (TNF) ligand] TNF-related apoptosis-inducing ligand (TRAIL).

48. (Once Amended) The isolated polynucleotide of claim 35, wherein said first nucleic acid encodes a polypeptide which induces apoptosis.

81. (Once Amended) An isolated polynucleotide comprising a first nucleic acid at least 90% identical to a second [reference] nucleic acid encoding amino acids 134 to 157 of SEQ ID NO:2.

82. (Once Amended) The isolated polynucleotide of claim 81, wherein said first nucleic acid is at least 95% identical to said second [reference] nucleic acid.

83. (Once Amended) The isolated polynucleotide of claim 82, which [comprises a nucleic acid encoding] encodes amino acids 134 to 157 of SEQ ID NO:2.

93. (Once Amended) A host cell comprising the isolated polynucleotide of claim [85]  
81.

96. (Once Amended) An isolated polynucleotide comprising a first nucleic acid at least 90% identical to a second [reference] nucleic acid encoding amino acids 158 to 360 of SEQ ID NO:2.

97. (Once Amended) The isolated polynucleotide of claim 96, wherein said first nucleic acid is at least 95% identical to said second [reference] nucleic acid.

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98. (Once Amended) The isolated polynucleotide of claim 97, which [comprises a nucleic acid encoding] encodes amino acids 158 to 360 of SEQ ID NO:2.

C8 Sub D1

100. (Once Amended) The isolated polynucleotide of claim 96, wherein said first nucleic acid encodes a polypeptide [which] fragment which is capable of functioning as part of a mature DR5 polypeptide to induce [induces] apoptosis.

114. (Once Amended) An isolated polynucleotide comprising a first nucleic acid at least 90% identical to a second [reference] nucleic acid encoding amino acids 273 to 340 of SEQ ID NO:2.

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115. (Once Amended) The isolated polynucleotide of claim 114, wherein said first nucleic acid is at least 95% identical to said second [reference] nucleic acid.

116. (Once Amended) The isolated polynucleotide of claim 115, which [comprises a nucleic acid encoding] encodes amino acids 273 to 340 of SEQ ID NO:2.

Sub D2

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118. (Once Amended) The isolated polynucleotide of claim 114, wherein said first nucleic acid encodes a polypeptide [which] fragment which is capable of functioning as part of a mature DR5 polypeptide to induce [induces] apoptosis.

132. (Once Amended) An isolated polynucleotide comprising a first nucleic acid at least 90% identical to a second [reference] nucleic acid encoding the mature amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97920.

133. (Once Amended) The isolated polynucleotide of claim 132, wherein said first nucleic acid is at least 95% identical to said second [reference] nucleic acid.

134. (Once Amended) The isolated polynucleotide of claim 133, [which comprises a] wherein said first nucleic acid [encoding] encodes the mature amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97920.

135. (Once Amended) The isolated polynucleotide of claim 132, wherein said second [reference] nucleic acid encodes the complete amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97920.

136. (Once Amended) The isolated polynucleotide of claim 135, [which comprises a] wherein said first nucleic acid [encoding] encodes the complete amino acid sequence encoded by the cDNA clone in ATCC Deposit No. 97920.

137. (Once Amended) The isolated polynucleotide of claim 132, wherein said first nucleic acid encodes a polypeptide which binds [a TNF ligand] TRAIL.

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138. (Once Amended) ~~The isolated polynucleotide of claim 132, wherein said first nucleic acid encodes a polypeptide which induces apoptosis.~~

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152. (Once Amended) ~~An isolated polynucleotide comprising 30 contiguous nucleotides of nucleotides [284] 754 to 1362 of SEQ ID NO:1.~~

153. (Once Amended) ~~The isolated polynucleotide of claim 152, comprising 50 contiguous nucleotides of nucleotides [284] 754 to 1362 of SEQ ID NO:1.~~

C13 <sup>Sub D3</sup>

155. (Once Amended) ~~The isolated polynucleotide of claim 152, which encodes a polypeptide [which] fragment which is capable of functioning as part of a mature DR5 polypeptide to induce [induces] apoptosis.~~

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165. (Once Amended) ~~A host cell comprising the isolated polynucleotide of claim [154] 155.~~

C15

168. (Once Amended) ~~A method of producing a polypeptide comprising culturing the host cell of claim [165] 163 under conditions such that said polypeptide is expressed, and recovering said polypeptide.~~

169. (Once Amended) ~~An isolated polynucleotide comprising a nucleic acid which encodes at least [7] 50 contiguous amino acids of amino acids 1 to 360 of SEQ ID NO:2;~~

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wherein said at least [7] 50 contiguous amino acids bind an antibody with specificity for the polypeptide [encoded by] consisting of amino acids 1 to 360 of SEQ ID NO:2.

186. (Once Amended) An isolated polynucleotide comprising a nucleic acid which hybridizes to nucleotides [284] 754 to 1362 of SEQ ID NO:1, or the complement thereof, under conditions comprising:

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(a) incubating overnight at 42°C in a solution consisting of 50% formamide, 5x SSC, 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA; and

(b) washing at 65°C in a solution consisting of 0.1x SSC;

wherein said nucleic acid is at least 15 nucleotides in length.

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C17

191. (Once Amended) The isolated polynucleotide of claim 186, wherein said nucleic acid hybridizes to the complement of nucleotides 754 to 1362 of SEQ ID NO:1, and wherein said nucleic acid encodes a polypeptide [which] fragment which is capable of functioning as part of a mature DR5 polypeptide to induce [induces] apoptosis.

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201. (Once Amended) A host cell comprising the isolated polynucleotide of claim [190] 191.

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205. (Once Amended) An isolated polynucleotide comprising a first nucleic acid at least 90% identical to a second [reference] nucleic acid encoding at least 30 contiguous amino acids from [1] 158 to 360 of SEQ ID NO:2.

206. (Once Amended) The isolated polynucleotide of claim 205, wherein said first nucleic acid is at least 95% identical to said second [reference] nucleic acid.

207. (Once Amended) The isolated polynucleotide of claim 206, wherein said first nucleic acid encodes at least 30 contiguous amino acids from [1] 158 to 360 of SEQ ID NO:2.

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208. (Once Amended) The isolated polynucleotide of claim 206, wherein said second [reference] nucleic acid encodes at least 50 contiguous amino acids from [1] 158 to 360 of SEQ ID NO:2.

209. (Once Amended) The isolated polynucleotide of claim 208, wherein said first nucleic acid encodes at least 50 contiguous amino acids from [1] 158 to 360 of SEQ ID NO:2.

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211. (Once Amended) The isolated polynucleotide of claim 205, wherein said first nucleic acid encodes a polypeptide [which] fragment which is capable of functioning as part of a mature DR5 polypeptide to induce [induces] apoptosis.

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221. (Once Amended) A host cell comprising the isolated polynucleotide of claim [210] 211.

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224. (Once Amended) A method of producing a polypeptide comprising culturing the host cell of claim [221] 219 under conditions such that said polypeptide is expressed, and recovering said polypeptide.



Kindly add the following claims:

--225. An isolated polynucleotide comprising a nucleic acid which encodes a polypeptide at least 90% identical to amino acids 1 to 133 of SEQ ID NO:2.

226. The polynucleotide of claim 225, wherein said polypeptide is at least 95% identical to amino acids 1 to 133 of SEQ ID NO:2.

227. The polynucleotide of claim 226, wherein said nucleic acid encodes amino acids 1 to 133 of SEQ ID NO:2.

228. The polynucleotide of claim 227, which comprises nucleotides 283 to 681 of SEQ ID NO:1.

229. The polynucleotide of claim 225, wherein said nucleic acid encodes a polypeptide which binds TRAIL.

230. The polynucleotide of claim 225, further comprising a heterologous polynucleotide.

231. The polynucleotide of claim 230, wherein said heterologous polynucleotide encodes a heterologous polypeptide.

232. The polynucleotide of claim 231, wherein said heterologous polypeptide comprises an immunoglobulin Fc region.

233. The polynucleotide of claim 232, wherein said immunoglobulin Fc region is a human immunoglobulin Fc region.

234. A method of producing a vector that comprises inserting the polynucleotide of claim 225 into a vector.

235. A vector comprising the polynucleotide of claim 225.

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236. The vector of claim 235, wherein said polynucleotide is operably associated with a heterologous regulatory sequence.

237. A host cell comprising the polynucleotide of claim 225.

238. The host cell of claim 237, wherein said polynucleotide is operably associated with a heterologous regulatory sequence.

239. A host cell comprising the polynucleotide of claim 229.

240. The host cell of claim 239, wherein said polynucleotide is operably associated with a heterologous regulatory sequence.

241. A method of producing a polypeptide comprising culturing the host cell of claim 239 under conditions such that said polypeptide is expressed, and recovering said polypeptide.

242. An isolated polynucleotide comprising a nucleic acid which encodes a polypeptide selected from the group consisting of:

a polypeptide consisting of amino acids 11 to 59 of SEQ ID NO:2;

a polypeptide consisting of amino acids 68 to 103 of SEQ ID NO:2;

a polypeptide consisting of amino acids 173 to 220 of SEQ ID NO:2; and

a polypeptide consisting of amino acids 224 to 319 of SEQ ID NO:2;

wherein said polypeptide bind an antibody with specificity for the polypeptide consisting of amino acids 1 to 360 of SEQ ID NO:2.

243. The polynucleotide of claim 242, wherein said nucleic acid encodes amino acids 11 to 59 of SEQ ID NO:2.

244. The polynucleotide of claim 242, wherein said nucleic acid encodes amino acids 68 to 103 of SEQ ID NO:2.

245. The polynucleotide of claim 242, wherein said nucleic acid encodes amino acids 173 to 220 of SEQ ID NO:2.

246. The polynucleotide of claim 242, wherein said nucleic acid encodes amino acids 224 to 319 of SEQ ID NO:2.

247. The polynucleotide of claim 242, further comprising a heterologous polynucleotide.

248. The polynucleotide of claim 247, wherein said heterologous polynucleotide encodes a heterologous polypeptide.

249. The polynucleotide of claim 248, wherein said heterologous polypeptide comprises an immunoglobulin Fc region.

250. The polynucleotide of claim 249, wherein said immunoglobulin Fc region is a human immunoglobulin Fc region.

251. A method of producing a vector that comprises inserting the polynucleotide of claim 242 into a vector.

252. A vector comprising the polynucleotide of claim 242.

253. The vector of claim 252, wherein said polynucleotide is operably associated with a heterologous regulatory sequence.

254. A host cell comprising the polynucleotide of claim 242.

255. The host cell of claim 254, wherein said polynucleotide is operably associated with a heterologous regulatory sequence.

256. A method of producing a polypeptide comprising culturing the host cell of claim 254 under conditions such that said polypeptide is expressed, and recovering said polypeptide.

257. An isolated polynucleotide comprising a nucleic acid which hybridizes to the complement of nucleotides 284 to 1362 of SEQ ID NO:1 under conditions comprising:

(a) incubating overnight at 42°C in a solution consisting of 50% formamide, 5x SSC, 50 mM sodium phosphate (pH 7.6), 5x Denhardt's solution, 10% dextran sulfate, and 20 µg/ml denatured, sheared salmon sperm DNA; and

(b) washing at 65°C in a solution consisting of 0.1x SSC;

wherein said polynucleotide encodes a polypeptide selected from the group consisting of:  
a polypeptide which binds TRAIL, and  
a polypeptide which induces apoptosis.

258. The polynucleotide of claim 257, which encodes a polypeptide which binds TRAIL.

259. The polynucleotide of claim 257, which encodes a polypeptide which induces apoptosis.

260. The polynucleotide of claim 257, further comprising a heterologous polynucleotide.

261. The polynucleotide of claim 260, wherein said heterologous polynucleotide encodes a heterologous polypeptide

262. The polynucleotide of claim 261, wherein said heterologous polypeptide comprises an immunoglobulin Fc region.

263. The polynucleotide of claim 262, wherein said immunoglobulin Fc region is a human immunoglobulin Fc region.

264. A method of producing a vector that comprises inserting the polynucleotide of claim 257 into a vector.

265. A vector comprising the polynucleotide of claim 257.

266. The vector of claim 265, wherein said polynucleotide is operably associated with a heterologous regulatory sequence.

267. A host cell comprising the polynucleotide of claim 257.

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268. The host cell of claim 267, wherein said polynucleotide is operably associated with a heterologous regulatory sequence.

269. A method of producing a polypeptide comprising culturing the host cell of claim 267 under conditions such that said polypeptide is expressed, and recovering said polypeptide.

270. An isolated polynucleotide comprising a nucleic acid which encodes a polypeptide at least 90% identical to 50 contiguous amino acids within amino acids 1 to 360 of SEQ ID NO:2.

271. The polynucleotide of claim 270, wherein said polypeptide is at least 95% identical to 50 contiguous amino acids within amino acids 1 to 360 of SEQ ID NO:2.

C23 272. The polynucleotide of claim 271, wherein said polypeptide encodes at least 50 contiguous amino acids within amino acids 1 to 360 of SEQ ID NO:2.

273. The polynucleotide of claim 270, wherein said nucleic acid encodes a polypeptide fragment capable of functioning as part of a DR5 extracellular domain to bind TRAIL.

274. The polynucleotide of claim 270, wherein said nucleic acid encodes a polypeptide fragment which is capable of functioning as part of a mature DR5 polypeptide to induce apoptosis.

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275. The polynucleotide of claim 270, further comprising a heterologous polynucleotide.

276. The polynucleotide of claim 275, wherein said heterologous polynucleotide encodes a heterologous polypeptide.

277. The polynucleotide of claim 276, wherein said heterologous polypeptide comprises an immunoglobulin Fc region.

278. The polynucleotide of claim 277, wherein said immunoglobulin Fc region is a human immunoglobulin Fc region.

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279. A method of producing a vector that comprises inserting the polynucleotide of claim 170 into a vector.

280. A vector comprising the polynucleotide of claim 270.

281. The vector of claim 280, wherein said polynucleotide is operably associated with a heterologous regulatory sequence.

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282. A host cell comprising the polynucleotide of claim 270.